Proposed plan of Ph. D. work on the topic

Bioprospecting of phytochemicals as anticancer agents.

submitted to the

Swami Ramanand Teerth Marathwada University

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BY

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Abstract of proposed work plan

Introduction

Medicinal plants are traditionally used for thousands of years, for several phytochemicals present in them and are integral part of herbal preparations of the Indian traditional health care system '*Ayurveda'*, these are named '*Rasayana'* for their proposed potential therapeutic properties. These phytochemicals contribute to preventing the development or progression of cancer. Anticancer therapy outlines the role of chemotherapy, diet, exercise, stress management and other several painful procedures in reducing chances for cancer progression. Current study is an attempt to understand the potential of phytochemicals to combat against the uncontrolled cell growth.

Aim and Objectives

The main aim of this study is to find out the novel compounds responsible for the anticancer activity from plants' origin.

Methodology

- Screening for novel compounds
- Extraction and Characterization of phytochemicals: Phytochemicals will be extracted in different solvents using sohxlet apparatus, and in sequential manner of decreasing polarity of solvents.

- Screening of novel compounds for anticancer potential: Separated compounds or crude extract will be sent for spectroscopic analysis by Mass spectroscopy. After the spectroscopy, identified compounds will be characterized as new or novel and checked for activities by comparing various chemical databases like PubChem, ChemSpider etc.
- Crude extracts or purified compounds will be checked for anticancer properties using different cell lines like breast cancer cell line MCF-7.

Importance of study / society applications

Plants are naturally gifted tools for the synthesis and isolation of medicinal compounds. The extraction and characterization of active compounds from medicinal plants have resulted in the discovery of new drugs with high therapeutic value (Wang H.Cao.et.al 1996). The utilization of medicinal plants (herbs) as a drug has long history throughout the world and herbal preparations, including herbal extracts, can be found in the pharmacopoeias of many countries [Jin Dai and Russell J. Mumpur2010]. In recent years there has been a renaissance of interest in natural or herbal remedies worldwide, partly because of the realization that modern medicine is not capable of providing a "cure-all" solution against human diseases and that the presence of unwanted side –effects is almost unavoidable [Maryam Zahin et al 2009]. Unlike modern drugs that invariably comprise a single active species, herbs extracts and/or prescriptions contain multiple active constituents. Interestingly, natural compounds contained in these "herbal cocktails" can act in a synergistic manner within the human body, and can provide unique therapeutic

properties with minimal or no undesirable side –effects [Tilak J.C.et al 2004]. Natural products could be organic or inorganic compounds that occur in various plant parts (shoot, root, leaves, bark, flowers and seeds) in a very highly diverse and extreme condition. The entire plant kingdom is an important source of natural compounds. Mainly carbohydrates, amino acids and proteins, are classified as primary metabolites, while others, such as alkaloids and phenolics, are classified as secondary metabolites [Ali.B.H et al 2008]. Secondary metabolites are essential to plant life; many of them act as a defense mechanism against bacterial, viral and fungal attack, analogous to the immune system of animals. A wide spectrum of natural products are created by combining different classes of compounds e.g. polyphenols and sugars to produce flavonoids and glycosides an important class of polyphenols. Substitutions with hydroxyl or ketones and additions with methyl or prenyl groups also increase the natural drug variety [6]. Some of the natural products also produce some toxic activity against living beings. Most of the natural products like flavonoids, saponins, terpenoids, steriods and coumarins etc are useful to cure various diseases and disorders of humans and animals. Natural product chemistry has been a topic of great interest since ancient times, being relevant to the preparation of food stuff, coloring matters, fibers, toxins and medicine etc [Beaurele et.al 2000]. The flavonoids represent an important group of pigments that occurs in the plant kingdom. The flavones, one of the flavonoids, possess interesting biological actions. The antioxidant activity of flavones is reported to be associated with those bearing hydroxyl functions [Ames B.N. et al 1995]. Numerous positive effects of flavonoids have been described, such as

antioxidant, antiviral, anticancer, anti-inflammatory, anti-alergic, anti-arthero genesis, anti-thrombosis and others. Next to their antioxidant capacity flavonoids can also contributes to a decrease in oxidative stress via inhibition or activation of key regulating enzymes such as xanthine oxidase, phospholipase and nitric oxide synthase. Furthermore, flavonoids may inhibit peroxynitrite formation by inhibiting inducible nitric oxide in activated macrophages, which is enhanced under certain stress conditions [Virendra et al 2013]. Different mechanism Flavonoids may provide remedy in radical mediated conditions of various stages of oxidative stress depending on their structures. [Rahman et al 2009]. Separation methods for the study of natural products have greatly stimulated the development of the refined techniques used today, such as analytical and preparative chromatographic methods (column chromatography, GC, TLC, HPTLC, HPLC and paper chromatography). These methods have made it possible for the isolation of extremely small quantities of bioactive natural compounds.

1.International status -

1.Jin Diel and Russel J. Mamper studied that natural phenolics have been found to intervene at all stages of cancer development.

2. Wel Zhong and shlow Y. Yang expressed that the herbs are effective potential source of natural antioxidant giving balance that herbs are more beneficial for health.

3.L Fernando reyes and leuis cisncros – zevallos found the temperature, ethylene, methyl, jasmonate and light treatment did not significantly effect the accumulation of phenolic compounds when compared to controlled samples.

4. V. katalinic. M. milos , t. kulisic ,m. jukie found that melissae foliu infusion have a significant reducing power and free radical scavenging ability in vitro when compared with red wine or beverages like tea.

5. S .Demiray ,M.E Pintado,P.M.L.Castro showed that acetone extracts of tiliaargentea had the highest antioxidant capacity as free ABTS radical scavengers.

2 . National Status

1.Nilam Jain, Shaily Goyal ,K.G. Ramawat. Antioxidant activity of medicinal plant play a very important role in postnatal recovery. So the medicinal plant are traditionally used in postpartum care.

2.Rangaswamy Raghupathi Raja Kannan, Radjassegarin Arumugam, Thirunavakarasu Thangarasjou, Perumal Annatharaman showed that H .Pinifolia and C. rotunda contains high levels of phenols ,flavonoids, tannin, vitamin C and E . These two sea grasses also shows good antioxidant and scavenging effect when compared to others.

3.C. Vijaya Kumar Reddy, D. Sreeramulu M. Raghunath .Their study expressed that the majority of fresh and dry fruits contains more phenolic antioxidents with potent free radical scavenging activity which are good for human health.

4.D. Sreeramlu, M. Raghunath their study showed that phenolic compounds may be significant contributor to AOA (on antioxidant activity) of the vegetables ,roots and tubers.

5.Madsen, H .L .and Bertelsen ,G. showed that spice as antioxidants. Trends in food science and technology.

Proposed work plan / formulations and structure of body_

Year wise plan of work

First year plan

1} Review of literature

2} Collection of the plant

3} Selections of the plant

4} Phytochemical screening

Second year plan

1} Qualitative Test for the Novel compounds.

2} Quantitative Test for Novel Compounds.

3} *TLC/ HPLC*

4} *Mass Spectroscopy*

5} *LC-MS*

Third year plan –

1} In vitro anti-cancer activity

2} In vitro anti-inflammatory activity

7 . References:

1. Ames, B.N., Gold, L.S., Willett, W.C., 1995. The causes and prevention of cancer. Proc. Natl. Acad. Sci. U. S. A. 92, 5258-5262.
2. Baeuerle, P.A., Rupec, R.A., Pahl, H.L., 1996. Reactive oxygen intermediates as second messengers of a general pathogen response. Pathol. Biol. (Paris) 44, 29Enroth, C., Eger, B.Y., Okamoto, K., Nishino, T., Pai, E.F., 2000. Crystal structures of bovine milk xanthine dehydrogenase and xanthine oxidase: structure-based mechanism of conversion [In Process Citation]. Proc. Natl. Acad. Sci. U. S. A. 97, 10, 723-728.
3. Hearse, D.J., Manning, A.S., Downey, J.M., Yellon, D.M., 1986. Xanthine oxidase: a critical mediator of myocardial injury during ischemia and reperfusion? Acta Physiol. Scand., Suppl. 548, 65-70.
4. Houston, M., Estevez, A., Chumley, P., Aslan, M., Marklund, S., Parks, D.A., Freeman, B.A., 1999. Binding of xanthine oxidase to vascular endothelium. Kinetic characterization and oxidative impairment of nitric oxide-dependent signaling. J. Biol. Chem. 274, 4985-4980.

5. Houston, M., Estevez, A., Chumley, P., Aslan, M., Marklund, S., Parks, D.A., Freeman, B.A., 1999. Binding of xanthine oxidase to vascular endothelium. Kinetic characterization and oxidative impairment of nitric oxide-dependent signaling. J. Biol. Chem. 274, 4985-4980.
6. Parks, D.A. and D.N. Granger, Xanthine oxidase: biochemistry, distribution and physiology. Acta Physiol Scand Suppl, 1986. 548: 87-99.
7. Borges, E.F., and Roleira, F. Progress towards the discovery of xanthine oxidase inhibitors. Current Medicinal Chemistry, 2002. 9: 195-217.
8. Hille, R. and T. Nishino, Flavoprotein structure and mechanism. 4. Xanthine oxidase and xanthine dehydrogenase. Faseb J, 1995. 9(11): 995-1003.
9. Wang .H :Cao. G ; prior R. L . Total anticancer capacity of fruits J. Agric,food chem..1996
10. Jin Dai and Russell J.Mumpur (2010). Plant phenolics; extraction,analysis and their antioxidant and anticancer properties, Molucules 2010:7313-7353.
11. Maryam Zahin. Farrukhaquil .The in vitro antioxidant activity and total phenolic content of four Indian medicinal plants.IJPPS 2009.
12. Tilak J .C, Adhikari S, Devasagayam TP (2004): Anticancer properties of plumbago-zylanica , an Indian medicinal plants and its active ingredients,plumbagin Rep.9 219-227.

Student Signature **Guide Signature**

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